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IN THE UNITED STATES RECEIVING OFFICE (US/RO)

Applicant: Bruno Tocque et al. Customer No: 21559

Serial No:

Filed: March 5, 2002

Titled: METHODS AND COMPOSITIONS FOR DETECTING PATHOLOGICAL EVENTS

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PRELIMINARY AMENDMENT

Prior to examination, kindly amend the above-referenced application as follows:

In the Specification

On page 1, after the title, insert the following paragraph:

--Cross Reference To Related Applications

This application is a continuation of U.S.S.N. 09/456,461, filed December 8, 1999. This application also claims priority from French application serial no. 99/11563, filed September 16, 1999, and international application serial no. PCT/FR00/02439, filed on September 9, 2000.--

In the claims

Please cancel claims 1-26 and add the following new claims:

27. A process for the detection *in vitro* of the presence of a pathological condition in a subject, comprising (i) providing a sample of blood cells from the subject, wherein said blood cells comprise lymphocytes, macrophages, monocytes or dendritic cells, (ii) preparing nucleic acids from the sample and (iii) hybridizing all or part of the nucleic acids so prepared with at least one nucleic acid library in order to obtain a hybridization profile, the nucleic acid library comprising a plurality of nucleic acid clones specific for splicing forms of genes, the splicing forms being characteristic of blood cells in said pathological condition, the hybridization profile indicating the presence of blood cells in the sample characteristic of the pathological condition, thereby detecting the presence of said pathological condition in said subject.

28. The process according to claim 27, wherein at least one library further comprises nucleic acids specific for genes whose level of expression is modified in a blood cell in a pathological situation.

29. The process according to claim 27, wherein at least one library is deposited on a support.

30. The process according to claim 27, wherein the nucleic acids prepared from the sample are total or messenger RNA or cDNA derived therefrom.

31. The process according to claim 30, wherein the nucleic acids prepared from the sample are amplified.

32. The process according to claim 27, wherein the nucleic acids are labeled.

33. The process according to claim 27, for the detection *in vitro* of the stage of progression or the site of a pathology in a subject.

34. A process of detection *in vitro* of blood cells characteristic of the presence of a pathological condition, comprising (i) providing a sample of blood cells from the subject, wherein said blood cells comprise lymphocytes, macrophages, monocytes or dendritic cells, (ii) preparing nucleic acids from the sample and (iii) hybridizing all or part of the nucleic acids so prepared with at least one nucleic acid library in order to obtain a hybridization profile, the nucleic acid library comprising a plurality of nucleic acid clones specific for splicing forms of genes, the splicing forms being characteristic of blood cells in said pathological condition, the hybridization profile indicating the presence of blood cells in the sample characteristic of the pathological condition.

35. A process of preparation of a nucleic acid library characteristic of a pathological condition, wherein said process comprises (i) obtaining a first nucleic acid preparation from blood cells isolated from an organism presenting a pathology,

said blood cells comprising lymphocytes, macrophages, monocytes or dendritic cells, (ii) obtaining a reference nucleic acid preparation from blood cells isolated from an organism not presenting said pathology, (iii) hybridizing said first preparation and said reference preparation and (iv) recovering, from the hybrids formed in (iii), nucleic acids characteristic of blood cells from the organism in a pathological condition.

36. The process of claim 35, for preparing a library of nucleic acids characteristic of the stage of progression of a pathology, wherein the first nucleic acid preparation is obtained from blood cells isolated from an organism presenting a pathology at a defined stage of progression and the reference nucleic acid preparation is obtained from blood cells isolated from an organism presenting said pathology at a different stage of progression.

37. The process according to claim 35, comprising the recovery of clones of non-hybridized nucleic acids.

38. The process according to claim 35, comprising the recovery, from the hybrids formed, of nucleic acid clones specific for splicing forms of genes.

39. The process according to claim 35, wherein the library is deposited on a support.

40. A library of nucleic acid clones, wherein said library comprises nucleic acid clones specific for genes whose level of expression or splicing is modified in a blood cell from an organism in a pathological situation.

41. The library of claim 40, wherein said pathological situation is a cancer or a neurodegenerative disease.

42. The kit usable for the implementation of a process according to claim 27, comprising a nucleic acid library comprising nucleic acids specific for splicing forms of genes characteristic of blood cells from an organism in a pathological situation.

43. A process for the detection *in vitro* of the presence of a disease in a subject, comprising (i) the preparation of proteins from a sample of blood cells from said subject and, (ii) the determination of the presence, in said preparation (i), of a protein or protein domain characteristic of said disease, said presence indicating the presence of said disease in said subject.

REMARKS

The specification was amended in order to incooporate the priority information into the text. Claims 1-26 were canceled and replaced with claims 27-43 in order to place them in the most appropriate form for the U.S. No new matter has bee added by any of the above amendments.

If there are any charges or credits not covered, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: March 5, 2002

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